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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,235	08/27/2001	Girish Sahni	07064-009002	5356

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,235	SAHNI ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,32 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0.0

DETAILED ACTION

Applicant's Request for Continuing Examination and amendment received April 20, 2005, in response to the Final Rejection of December 16, 2004 and the Advisory Action of March 9, 2005 is acknowledged. It is acknowledged that applicants have canceled Claim 1 and amended Claims 3, 32, and 33. Claims 3, 32, and 33 are pending and are hereby reconsidered.

Specification-Objections

The specification is objected to for the following reasons.

Line 1 of the specification is objected to for not stating the status of parent Application 09/471,349 as abandoned on September 21, 2001.

The specification on page 8, paragraph 2, states:

> "It is known that of the 414 residues constituting native SK, only the first 15 residues and the last 31 residues are expendable, with the resultant truncated polypeptide being nearly as active as the native full-length protein in terms of PG activation ability (Jackson, K.W., and Tang, J. (1982) *Biochemistry* 21; 6620)."

However, Jackson et al, 1982 do not teach that the first 15 and last 31 residues of streptokinase are expendable.

On page 37, as set forth in the amendment of April 9, 2002, the reverse primer (MY 14) has an error. The sequence switches near the 3' end from reverse complement to coding sequence, i.e. GGG GC**G TCTA** (the bold is coding sequence).

On page 45, as set forth in the amendment of April 9, 2002, the designation for the MY-10 primer is incorrect. Line 2 of the paragraph states that the MY-10 primer is "SK sequence (codons 377-383; Cf Fig 3)". This does not agree with the sequence set forth in the following lines, i.e., 5'G-TAC-GGA-TCC... etc.

There is a large blank space on page 44.

The specification is objected to for not disclosing the structure of the fusion proteins used in the experiment of Figure 24.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object i.e. "We claim" or "The claims are".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both Claim 3 and 32 have improper antecedent usage and, therefore, a person of ordinary skill in the art would not know the metes and bounds of the recited inventions. For Claim 3, line 2, the phrase "the time lag ranges between 5 to 30 minutes" lacks antecedent basis in either Claim 3 or Claim 33, from which it depends. For Claim 32, line 1-2, the phrase "a genetically engineered hybrid polypeptide plasminogen activator of claim 33" should be "the genetically engineered hybrid polypeptide plasminogen activator of claim 33".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 32, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 3, 32, and 33 introduce the limitation of a hybrid polypeptide comprising residues 16-383 of SEQ ID NO: 2. The specification fails to describe said limitation and, thus, Claims 3, 32, and 33 are rejected under 35 U.S.C. 112, first paragraph, for introducing New Matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 32, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al, 1995 in view of Matsuka et al, 1994 (IDS) and further in view of Goldstein et al, 1996. Dawson et al teach a fusion protein comprising residues 16-383 of streptokinase of SEQ ID NO: 2 (Example 5). Dawson et al do not teach a fusion protein comprising residues 16-383 of streptokinase of SEQ ID NO: 2 and either or both of the 1/2 and 4/5 fibrin binding domain pairs set forth by residues 1-106 and 150-259 of SEQ ID NO: 4, respectively. Matsuka et al teach that the fourth and fifth fibrin binding domains of fibronectin consist of residues 150-259 of SEQ ID NO: 4 (Table 1), which forms the critical fibrin-binding site of the Fib-1 region of fibronectin (pg 9544, parg 2; Fig 9). It would have been obvious to a person of ordinary skill in the art to use the method of Dawson et al to prepare a fusion protein comprising the streptokinase core of residues 16-383 of SEQ ID NO: 2 linked to the fibrin binding domains 4/5 set forth by

residues 150-259 of SEQ ID NO: 4. Motivation to do so is provided by Dawson et al wherein they teach the following. Fibrinolytic therapy using streptokinase and other plasminogen activators has become widespread (col 1, lines 39-42). A major problem with these agents is that they are not thrombus specific, as they activate plasminogen in the general circulation (col 1, lines 49-52). An approach to enhancing fibrinolysis and inhibition of blood clotting is based on the use of fusion proteins that are activated specifically at the site of blood clotting (col 2, lines 1-5). Goldstein et al teach that one method of targeting streptokinase activity to the site of blood clotting is to use a fusion protein comprising streptokinase and an anti-fibrin antibody (Fig 6). A person of ordinary skill in the art would know that the fibrin binding domain set forth by residues 150-259 of SEQ ID NO: 4 would serve the same targeting function as the anti-fibrin antibody of Goldstein et al. Therefore, based on the problem to be solved, the state of the art, and knowledge of the skilled artisan, Claims 3, 32, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al, 1995 in view of Matsuka et al, 1994 (IDS) and further in view of Goldstein et al, 1996.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.